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Rivas, Ioar

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Associations between sources of particle number and mortality in four European cities

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ABSTRACT

Background: The evidence on the association between ultrafine (UFP) particles and mortality is still inconsistent. Moreover, health effects of specific UFP sources have not been explored. We assessed the impact of UFP sources on daily mortality in Barcelona, Helsinki, London, and Zurich.

Methods: UFP sources were previously identified and quantified for the four cities: daily contributions of photonucleation, two traffic sources (fresh traffic and urban, with size mode around 30 nm and 70 nm, respectively), and secondary aerosols were obtained from data from an urban background station. Different periods were investigated in each city: Barcelona 2013–2016, Helsinki 2009–2016, London 2010–2016, and Zurich 2011–2014. The associations between total particle number concentrations (PNC) and UFP sources and daily (natural, cardiovascular [CVD], and respiratory) mortality were investigated using city-specific generalized linear models (GLM) with quasi-Poisson regression.

Results: We found inconsistent results across cities, sources, and lags for associations with natural, CVD, and respiratory mortality. Increased risk was observed for total PNC and natural mortality in Helsinki (lag 2; 1.3% [0.07%, 2.5%]), CVD mortality in Barcelona (lag 1; 3.7% [0.17%, 7.4%]) and Zurich (lag 0; 3.8% [0.31%, 7.4%]), and respiratory mortality in London (lag 3; 2.6% [0.84%, 4.45%]) and Zurich (lag 1; 9.4% [1.0%, 17.9%]). A similar pattern of associations between health outcomes and total PNC was followed by the fresh traffic source, for which we also found the same associations and lags as for total PNC. The urban source (mostly aged traffic) was associated with respiratory mortality in Zurich (lag 1; 12.5% [1.7%, 24.2%]) and London (lag 3; 2.4% [0.90%, 4.0%]) while the secondary source was associated with respiratory mortality in Zurich (lag 1: 12.0% [0.63%, 24.5%]) and Helsinki (4.7% [0.11%, 9.5%]). Reduced risk for the photonucleation source was

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observed for respiratory mortality in Barcelona (lag 2, −8.6% [−14.5%, −2.4%]) and for CVD mortality in Helsinki, as this source is present only in clean atmospheres (lag 1, −1.48 [−2.75, −0.21]).
Conclusions: We found inconsistent results across cities, sources and lags for associations with natural, CVD, and respiratory mortality.

1. Background

Epidemiological and toxicological evidence suggests that short and long-term exposure to particulate matter (PM) has a negative impact upon human health (WHO, 2013), with 4.2 million deaths per year attributed to exposure to outdoor air pollution (WHO, 2018).

The associations between different size fractions of PM, such as PM measured as mass with an aerodynamic diameter ≤10 μm (PM_{10}) and ≤2.5 μm ($PM_{2.5}$), and mortality have been largely established (Liu et al., 2019; Ostro et al., 2011; Samoli et al., 2013; Schwartz et al., 2018; among others). Attempts have also been made to identify which sources or chemical constituents were leading the associations (Atkinson et al., 2010; Heo et al., 2014; Perez et al., 2009; Thurston et al., 2016).

Much less information is available on the effects on mortality of ultrafine particles (UFP; usually defined as particles <100 nm and commonly measured as particle number concentrations, PNC) even though biological and physical reasons suggest that negative health effects may be accentuated for the smaller particle sizes (Meng et al., 2013; Sioutas et al., 2005). Although some positive associations between short-term exposure to UFP and mortality have been reported (Breitner et al., 2011; Stölzel et al., 2007), many of the studies reported weak or no evidence (Atkinson et al., 2010; Braniš et al., 2010; Lanzinger et al., 2016; Stafoggia et al., 2017). These inconsistencies may be due to (1) the difficulty in accurately estimating the exposure due to the large change over short distances of UFP number concentrations (Zhu et al., 2002) and to (2) a different relative and absolute contribution of the sources of UFP on the different days (Tobías et al., 2018). However, there is a lack of studies evaluating the associations between source-specific UFP and mortality. Firstly, because UFP data collection is relatively new compared with other metrics but also because determining the sources is not an easy task for PNC.

The quantification of the different sources affecting UFP and disentangling the impact on public health of each of these sources would allow targeted policies to reduce emissions. To account for all this, we have collected data from four European cities characterized by different climatic conditions, emission sources, and urban morphology, on ultrafine particle number concentrations and their source contributions (exposure data) and daily counts of all-cause non-accidental, cardiovascular (CVD), and respiratory deaths (health outcome data).

To our knowledge, no epidemiological study on the association of specific sources of UFP and mortality rates has been conducted before. To evaluate the short-term effects of each source and its total PNC on mortality we have used a time-series design, investigating the associations between the different sources of ultrafine particles and daily death counts in four European Cities (Barcelona, Helsinki, London, and Zurich) at different lag times.

2. Methods

2.1. Description of the data

2.1.1. Mortality data

Data were collected for Barcelona, Helsinki, London, and Zurich. The selection of the cities and the period of analysis was limited to the availability of long-term measurements of particle number size distributions (PNSD).

For each city, data were collected on daily counts of all-cause non-accidental (ICD-10 Chapters A-R), cardiovascular (CVD; ICD-10 Chapter I), and respiratory (ICD-10 Chapter J) deaths with regards to the resident population of the city. Data were obtained from the official services for health statistics.

Barcelona

Barcelona (Spain) is a coastal location with 1.6 million inhabitants (3.6 million in the metropolitan area; 2016; Eurostat, 2018). Mortality data was collected for the period 2013–2016 (four years) for the city of Barcelona and surrounding cities from the metropolitan area that are close (within a 6 km radius) to the air quality monitoring station located in the south-west of Barcelona city (Hospitalet Llobregat, Esplugues de Llobregat, Sant Just Desvern, Sant Feliu de Llobregat, Cornellà de Llobregat, and Sant Joan Despí). The total population of the area of study is 2.1 million (IDESCAT, 2019). Mortality data were collected from the Health Department (Departament de Salut) of the Catalan Government.

Helsinki

Helsinki is also a coastal city located in the South of Finland. Helsinki has 0.6 million inhabitants (1.1 million in the metropolitan area; 2016; Eurostat, 2018) which makes it the largest city in Finland. We obtained mortality data for the Helsinki metropolitan area (Espoo, Helsinki, Vantaa, Kauniainen) for the period 2007–2016 (ten years) from Statistics Finland (Tilastokeskus).

London

Greater London is the largest city in the United Kingdom and in Europe with 8.7 million inhabitants (Eurostat, 2018). We collected mortality data from the UK Office for National Statistics (ONS) for the period 20th January 2010–30th September 2016 (almost seven years).

Zurich

Zurich has 0.4 million inhabitants and is the largest city in Switzerland (2014; BFS, 2018). Mortality data were obtained for the municipality of Zurich and another 89 communes (listed in Table S1) that are part of the Zurich metropolitan area. The total population for the area included in the study is 1.1 million. The data for the 90 communes were obtained from the Swiss Federal Statistical Office (Bundesamt für Statistik, BFS) for the period December 2010–October 2014 (four years).

2.1.2. Ultrafine particle measurements, sources, and meteorological data

A detailed description of the instruments (Scanning Mobility Particle Sizer Spectrometers, SMPS, or Differential Mobility Particle Sizers, DMPS), measurements, and source apportionment with Positive Matrix Factorization (PMF) method is available in Rivas et al. (2020). Briefly, we obtained long-term time series of PNSD and gaseous pollutants (NO, NO_2, SO_2, O_3 and CO) from an urban background station in each city: Palau Reial in Barcelona (41°23′14″N, 02°06′56″E), SMEAR III Kumpula in Helsinki (60° 12′ 11″ N, 24° 57′ 40″ E), North Kensington in London (51°31′16″N, 00°12′48″W), and Kaserne in Zurich (47°22′39″N, 8°31′50″E). The particle size range measured varied across cities, being 11–478 nm in Barcelona (SMPS TSI 3936), 6–700 nm in Helsinki (DMPS), 17–640 nm in London (SMPS TSI 3080), and 10–487 nm in Zurich (SMPS TSI 3034).

PMF is a least-squares method developed by Paatero (1997) that is widely used in environmental sciences to identify and apportion the sources of particulate matter or PNSD observed at the receptor site. Sources of UFP were quantified by PMF applied to each size bin of hourly averaged PNSD as well as to gaseous data (NO_2, NO, SO_2, CO, O_3) since adding additional species (other than PNSD) can help to separate and identify the sources. We performed PMF with Multilinear Engine 2 (ME-2, Paatero, 1999) for each city separately and sources were identified and quantified for the periods of study (Rivas et al., 2020). With this technique, for each city we identified between 4 and 6 sources, with 2 or

3 being related to traffic emissions (from fresh to aged emissions). Here, for comparability among the cities, we are exploring the following sources (in increasing range of particle size):

Photonucleation: These are secondary particles of a very small size (<20 nm diameter) that are formed in the atmosphere from precursor gases (e.g. SO_2) due to reactions induced by the energy from solar radiation (Kulmala et al., 2000). Photonucleation processes are generally more common in clean atmospheres due to lower availability of particle surface for the gases to condense on (low condensation sink; Brines et al., 2015).

Fresh traffic: This source includes particles that nucleate (<20 nm, converted from gas to particle) right after and very close to the exhaust emission (also named delayed primary emissions; Rönkkö et al., 2017) as well as primary particles (directly emitted as particles) from vehicle exhaust emissions (small particles of around <60 nm). This source was directly identified in Barcelona, but for Helsinki, London, and Zurich it corresponds to the addition of the sources that were labelled as Traffic nucleation and Fresh Traffic in Rivas et al. (2020).

Urban: The main component of this source is aged traffic emissions (larger sizes than the particles in the Fresh Traffic source, approximately between 40 and 150 nm) but it also comprises a mix of other urban emissions such as biomass burning, heating, cooking and it includes large carbon agglomerates.

Secondary: These particles are aged particles that have grown due to the condensation of volatile gaseous compounds on their surface (approximately >80 nm, with a mode diameter around 200–300 nm). In contrast to primary particles, secondary particles become more relevant as they travel away from the source or in periods of the day, week or year with lower emissions (for example due to condensation of nitrate during night time; Poulain et al., 2011). These particles show the larger diameters within the PNSD.

In Helsinki, an extra source was identified related to biogenic emissions from the vegetation of the relatively close forests.

We also evaluated the associations between mortality and the total UFP number concentrations (**Total PNC**).

Temperature and relative humidity were collected at the air quality monitoring stations (or in a very close location) except for London, where meteorological data was collected at Heathrow Airport.

2.2. Statistical analysis

We evaluated the short-term effects of different sources of UFP and total PNC upon mortality with a time-series design. We investigated the associations between mortality and sources of UFP using generalized linear models (GLM) with quasi-Poisson regression. For our models, we used natural splines with city- and cause- specific degrees of freedom (df) as a smoothing function for time to control for long-term trend and seasonality. The df used for each city are reported in Table S2. For each city and cause of death, we tested using between 3 and 9 degrees of freedom (df) per year, and chose the df that minimized the sum of the absolute value of the Partial Autocorrelation Function (PACF) of the residuals (Peng et al., 2006). To control for weather: (i) we used thin plate regression splines within the Generalized Additive Model framework for relative humidity; (ii) temperature was controlled by two smooth terms in order to account for both high and low temperatures at different lags. Adjustment for high temperatures was done by fitting a natural spline with three df on the average temperature on the current and previous day (lag 0–1) only for the days when the lag 0–1 temperature was higher than the median annual temperature for the city. For low temperatures, we fitted a natural spline with two df for the average temperature on the previous 6 days (lag 1–6) only for the days when the temperature for the lag 1–6 was below the median annual temperature for the city (Samoli et al., 2016; Stafoggia et al., 2017). We also adjusted for an indicator variable for day of the week and for bank holiday. A different model was fitted for each lag. We investigated the effect of the same day exposure (lag 0) up to 5 days before (lag 5).

Single-source and multi-source (adjusting for the other sources) models were performed. We carried out a sensitivity analysis adjusting the models for NO_2 and O_3 (these analyses were only performed for total PNC because NO_2 and O_3 were used for the source apportionment). We could not evaluate the confounding effect of NO_2 and O_3 in London due to the difficulties in accessing the mortality data due to restrictions related to the SARS-CoV-2 pandemic.

Finally, we also performed the analyses by sex and for the population older than 75 years to test for effect modification.

Statistical analysis were carried out using R software (version 3.6.0; R Core Team, 2019).

3. Results

3.1. Contribution and correlation among the different sources

Source contribution data were missing for 371 (25%) of the 1461 days (4-year period) for Barcelona, 244 (7%) over 3,653 days (10-year period) for Helsinki, 548 days (22%) of the 2445 days (7-year period) for London, and 165 (12%) over 1,400 days (almost a 4-year period) for Zurich. Missing data was due to malfunctioning or calibration of the instrumentation or because the instrument was temporarily needed in other locations. Summary statistics for total PNC and the different source contributions are presented in Table 1. Time-series plots for total PNC and the different sources are presented in Fig. S1 and Pearson's correlation coefficients (r) in Table S3. Some sources showed a seasonal pattern: fresh traffic had increased concentrations in the colder months while photonucleation was especially notable during the summer periods. Total PNC was strongly correlated with the fresh traffic ($r > 0.81$) and with the urban source ($r > 0.61$) in all cities as these two sources are the main contributors to PNC. On the contrary, total PNC was weakly correlated with photonucleation ($r < 0.34$ in all cities) especially in London ($r = 0.09$). Moreover, photonucleation was weakly correlated with fresh traffic, urban, and secondary ($r < |0.30|$, with the correlation being either positive or negative depending on the city and the source). The correlation of total PNC and the different sources with $PM_{2.5}$ and PM_{10} is also shown in Table S3 (PM_{10} was not available for Helsinki nor $PM_{2.5}$ for Helsinki and Zurich). Total PNC showed no correlation with PM in Barcelona ($r = 0.25$ for $PM_{2.5}$, $r = 0.19$ for PM_{10}) and moderate correlation in London ($r = 0.58$ for both PM_{10} and $PM_{2.5}$) and Zurich ($r = 0.55$ for PM_{10}). Regarding the correlation with the sources, the secondary source showed a moderate correlation with PM in Barcelona ($r = 0.61$ for both fractions) and high in Zurich ($r = 0.83$ for PM_{10}). In London, the urban and the Secondary sources were highly correlated with PM_{10} and $PM_{2.5}$ ($r > 0.68$ in all cases) while there was no correlation with the other sources.

The absolute contributions of the sources are not directly comparable between cities, especially because the size range evaluated is different for each city. The difference is particularly important for photonucleation and fresh traffic sources, because these sources show the smallest size mode and the particle number concentrations are very dependent on the lower size cut of the instrument (it ranges between 6 nm in Helsinki and 17 nm in London).

Time-series plots and summary statistics for the mortality data are presented in Fig. S2 and Table 2, respectively. The median number of deaths per day from natural causes were 123, 49, 19, 21 for London, Barcelona, Helsinki and Zurich, respectively. For cardiovascular causes the median number of deaths per day were 37, 14, 7, and 7 and for respiratory causes 17, 5, 1, 1, respectively. In terms of population, Zurich and Helsinki are comparable (both with around 1.1 million inhabitants).

3.2. Individual GLM models

The results of the short-term associations between total PNC and the different UFP sources and natural death counts are illustrated in Fig. 1.

Table 1
Summary statistics for daily averages of Total PNC and the different sources contributing to UFP by city.

City (period) Size range)	UFP source (pt cm^{-3})	Mean (SD)	Min	Max	Median	IQR
Barcelona (01/2013–12/2016) 11–478 nm	Total PNC	11,371 (4,049)	3,165	29,416	10,780	5,601
	Photonucleation	2,601 (2,176)	0	12,434	2,190	2,875
	Fresh traffic	5,213 (2938)	74	18,512	4,649	3,582
	Urban	2,835 (1,414)	200	9,266	2,614	1,744
	Secondary	675 (481)	24	2,970	560	581
Helsinki (01/2007–12/2016) 6–700 nm	Total PNC	7,006 (3689)	815	37,019	6,205	4,012
	Photonucleation	315 (435)	0	4541	164	350
	Fresh traffic	3,264 (2378)	157	19,321	2,600	2,742
	Urban	2,222 (1569)	0	20,839	1,895	1,706
	Secondary	197 (186)	0	1,315	133	183
London (01/2010–09/2016) 17–640 nm	Total PNC	5,562 (2409)	1,339	21,422	5,210	2,921
	Photonucleation	211 (292)	0	2,060	93	263
	Fresh traffic	3,465 (1340)	746	10,467	3,320	1,818
	Urban	1,719 (1321)	94	11,485	1,332	1,429
	Secondary	166 (174)	0	1,157	98	170
Zurich (12/2010–10/2014) 10–487 nm	Total PNC	9,491 (4,054)	2,439	49,938	8,753	4,735
	Photonucleation	283 (306)	0	2548	196	321
	Fresh traffic	6,530 (3,054)	1,049	36,606	5,868	3,449
	Urban	2,426 (1,376)	248	11,782	2,149	1,739
	Secondary	316 (241)	0	2,026	257	301

Table 2
Summary statistics of (cause-specific) daily deaths by city.

CITY	AGE GROUP	PERIOD	NATURAL			CVD			RESPIRATORY		
			MIN	P50	MAX	MIN	P50	MAX	MIN	P50	MAX
Barcelona	All	2013–2016	24	49	87	3	14	34	0	5	19
Helsinki		2007–2016	5	19	43	0	7	20	0	1	6
London		2010–2016	76	123	215	18	37	74	4	17	54
Zurich		2011–2014	8	21	38	0	7	18	0	1	6
Barcelona	+75	2013–2016	16	37	66	2	12	28	0	4	16
Helsinki		2007–2016	1	16	31	0	5	16	0	0	5
London		2010–2016	47	81	152	9	26	54	2	13	44
Zurich		2011–2014	4	15	32	0	6	17	0	1	6

The estimates and confidence intervals for lag 0 to lag 2 are presented in Table S4. Most of the associations were null or with large 95% confidence intervals. Natural mortality was associated with an IQR increase of total PNC (1.3% [0.07%, 2.5%]) and fresh traffic (1.6% [0.20%, 3.1%]) at lag 2 and with secondary at lag 5 (1.1% [0.14%, 2.1%]) in Helsinki. In Barcelona, the associations showed a trend of increased risk for natural mortality and total PNC and the fresh traffic source from lag 1 to lag 3, but the associations were not significant (e.g. lag 1 for total PNC: 1.6% [−0.26%, 3.6%]). On the other hand, a reduced risk of natural mortality was observed at different lags for total PNC (lag 5: −0.93%, [−1.6%, −0.24%]), fresh traffic (lag 1: −1.2% [−2.0%, −0.41%]; lag 5: −0.84% [−1.6%, −0.08%]), urban traffic (lag 5: −0.66% [−1.3%, −0.04%]) and secondary (lag 3 to 5; e.g. lag 4: −0.73% [−1.3%, −0.12%]) in London. Reduced risk of natural mortality was also observed for the urban source at a lag 2 (−2.9% [−5.3%, −0.48%]) in Zurich.

The associations with cardiovascular mortality are presented in Fig. 2 and Table S5. An IQR increase in total PNC was associated with an increase of 3.7% [0.17%, 7.4%] of CVD deaths at lag 1 in Barcelona. CVD deaths in Zurich were also associated with total PNC (3.8% [0.31%, 7.4%]) and fresh traffic (3.5% [0.06%, 7.0%]) at lag 0. The estimates at lag 0 for the urban (3.1% [−1.0%, 7.3%]) and secondary sources (3.0% [−1.6%, 7.7%]) were also pointing towards an increased risk of CVD mortality. In Helsinki, a reduced risk of CVD mortality was observed for photonucleation at lag 1 (−1.5% [−2.7%, −0.21%]) and for secondary at lag 3 (−1.7% [−3.3%, −0.13%]). Most of the associations in London were null, however, a reduced risk of CVD mortality was observed for total PNC (−1.2% [−2.4%,-0.01%]) and fresh traffic (−1.6% [−2.9%, −0.22%]) at lag 3 and for the secondary source at lag 5 (−1.1 [−2.1%, −0.06%]).

The associations with respiratory mortality are presented in Fig. 3 and Table S6. Respiratory mortality was associated with total PNC (lag 1: 9.4% [1.0%, 17.9%]), fresh traffic (lag 1: 8.4% [0.43%, 16.5%]), urban (lag 0, 1 and 4; e.g. lag 1: 12.5% [1.7%, 24.2%]) and secondary (lag 1: 12.0% [0.63%, 24.5%]) in Zurich. Positive associations were also found for total PNC (2.6% [0.84%, 4.45%]) and the urban source (2.4% [0.90%, 4.0%]) at lag 3 in London and secondary particles at lag 0 in Helsinki (4.7% [0.11%, 9.5%]). Total PNC at lag 5 (−6.2% [−11.8%, −0.33%]) and photonucleation at lag 2 (−8.6% [−14.5%, −2.4%]) were associated with reduced risk of respiratory mortality in Barcelona.

The estimates for the different sources while being adjusted by the other sources (multi-source models) are presented in Table S4 (natural mortality), S5 (cardiovascular mortality), and S6 (respiratory mortality). The confidence intervals were wider in all cases when adjusted for the different sources and, in some cases, the absolute value for the estimates varied considerably. However, the general trend of the associations remained the same and similar results were obtained for all sources types and cause of mortality. We also obtained similar results when adjusting for deaths due to influenza (data not shown) and when adjusting for NO_2 and O_3 (separate models and only for total PNC; Fig. S3).

Finally, we did not find remarkable differences by sex or by restricting the analyses to people older than 75 years.

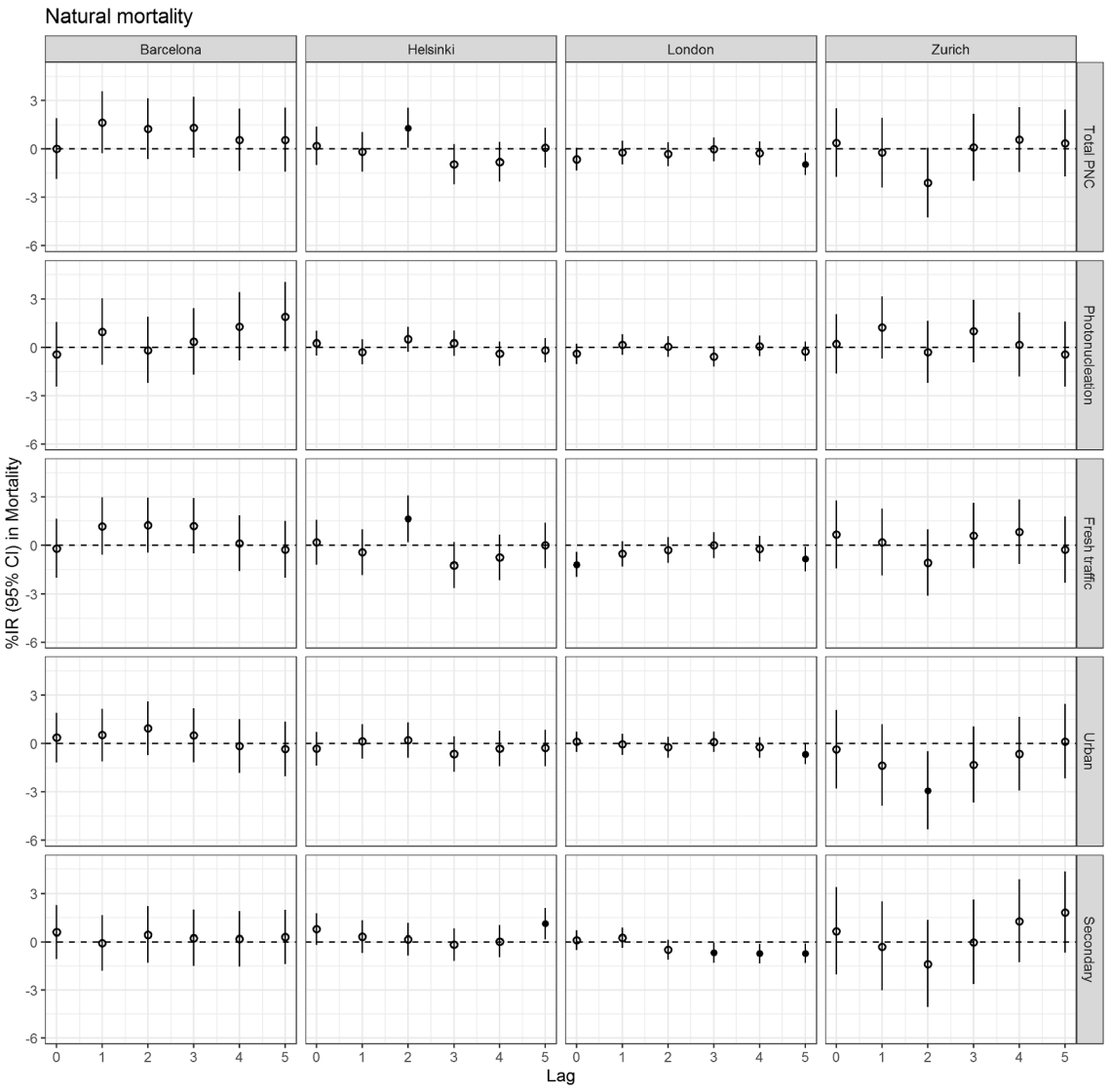

Fig. 1. Associations between natural mortality and total particle number concentrations (PNC) and the source contributions to ultrafine particles (photonucleation, fresh traffic, urban and secondary) from single lag models: percent increases of mortality (circles) and 95% confidence intervals (bars) per IQR increase at different lags.

4. Discussion

In this study, we investigated associations of total PNC and four different sources of UFP on the same day as the health event (lag 0) and up to 5 days before (lag 1 to lag 5) with daily mortality from natural, cardiovascular and respiratory causes. To the knowledge of the authors, this is the first study to evaluate the associations between specific sources of PNC and daily death counts. As a first step in the attempt to study the health effects of UFP by origin, in our previous publication (Tobías et al., 2018) we evaluated the associations of UFP according to their primary or secondary origin with daily death counts in different cities in Spain.

We found inconsistent results across cities, sources and lags for associations with natural, CVD, and respiratory mortality. Increased risk was observed for total PNC and natural mortality in Helsinki (lag 2), CVD mortality in Barcelona (lag 1) and Zurich (lag 0), and respiratory mortality in London (lag 3) and Zurich (lag 1). We also found a protective effect (negative estimates) in many lags and particularly for the city of London. However, these negative estimates are, *a priori*, not plausible and, if not due to chance, may be due to confounding by other pollutants. Also, London is the city with the largest area included in the analysis. Since UFP show large spatial variability, this may increase the likelihood that the spatial distribution is not constant across space on different days (higher spatial–temporal variation).

The analysis for respiratory and CVD in Helsinki and Zurich had low numbers of daily deaths and, therefore, potential low statistical power. However, in this type of analyses, what matters the most is the total number of deaths of the series, not the daily median (Armstrong et al., 2020).

Comparing our results with other publications is a difficult task as the particle size range may differ. The evidence available so far for the associations between PNC and (cause-specific) mortality is also inconsistent and weak in previous studies. For instance, some reported associations at shorter lags (lag 0, lag 1 or lag 0–1; Atkinson et al., 2010; Forastiere et al., 2005; Kettunen et al., 2007) while others reported associations at longer lags (lag 3 or larger; Stafoggia et al., 2017; Stölzel et al., 2007). Other studies reported no associations with mortality outcomes (Braniš et al., 2010). In general, the evidence is weak and inconsistent, even in studies including different cities with similar methodologies for the UFP measurements (Lanzinger et al., 2016; Stafoggia et al., 2017).

Regarding the patterns of the associations, Barcelona generally

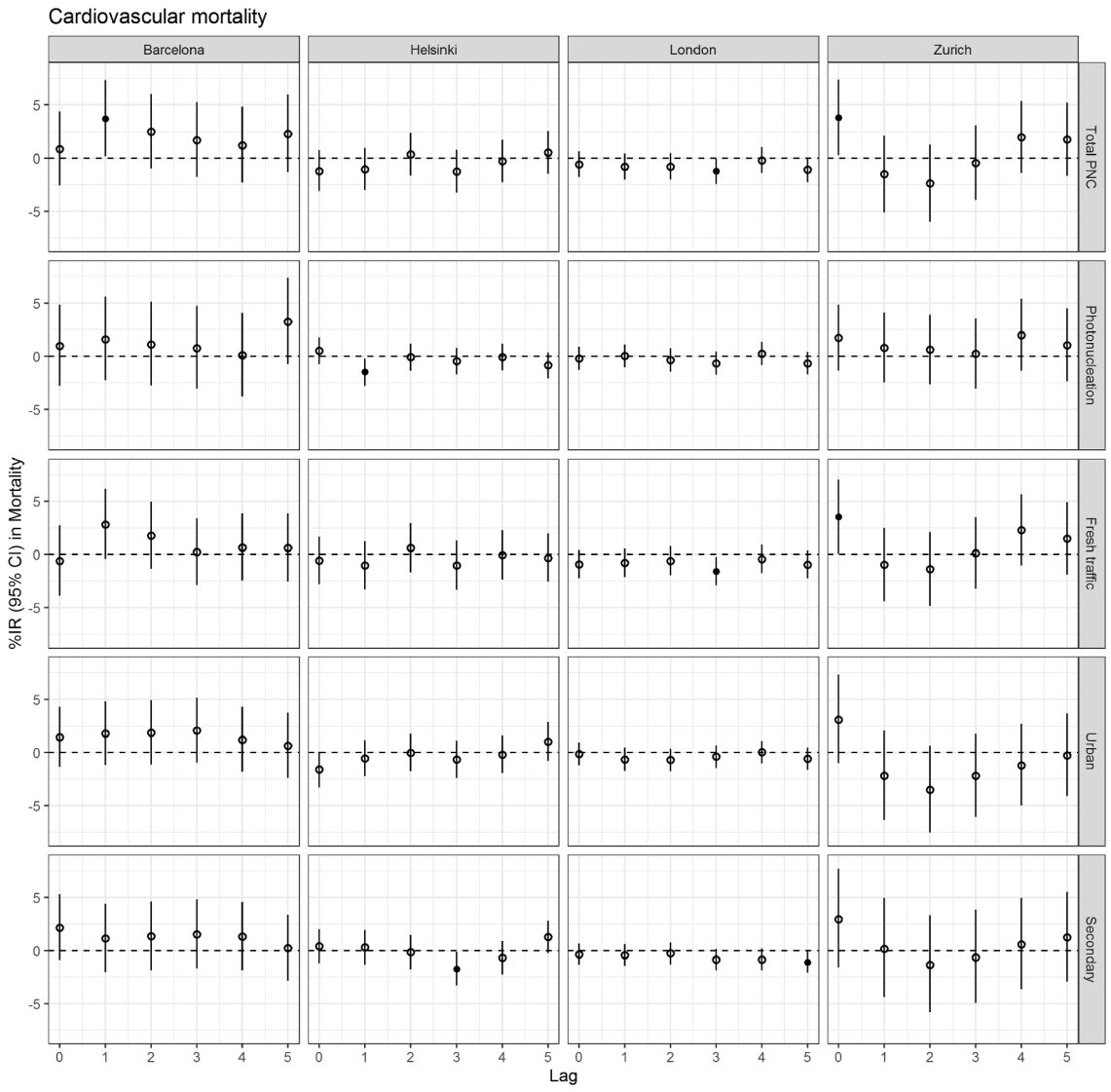

Fig. 2. Associations between cardiovascular (CVD) mortality and total particle number concentrations (PNC) and the source contribution to ultrafine particles (photonucleation, fresh traffic, urban and secondary) from single lag models: percent increases of mortality (circles) and 95% confidence intervals (bars) per IQR increase at different lags.

showed the highest estimates at lag 1 or 2 and it diminished for the following lags (lag 3-5) for total PNC and all the sources except Photonucleation. This type of pattern is commonly observed in time-series analysis. The pattern of associations in Helsinki usually showed an elevated risk at lag 2, which for some cases stands out from the rest of the associations (particularly for all-cause mortality). The opposite trend was observed in Zurich, where the patterns showed the lowest risk at lag 2. In London, the patterns were more varied for the different sources and causes of death, sometimes showing a flat M-like pattern.

One should be cautious when comparing the magnitude of the effects with other studies due to the heterogeneity of our data, which includes different cities with differences in the sources. For the effects of total PNC on mortality our estimates indicated an increase of around 1.3% for natural mortality, 3.8% for CVD mortality, and 2.4–9.4% for respiratory mortality (refer to Tables S4–S6 for the 95%CI) per IQR increases that range between 2,921 and 5,601pt cm^{-3} depending on the city (Table 1). Our estimates were larger but comparable (when considering the differences in the IQRs) with those of Atkinson et al. (2010) for London (UK) who reported increases of 1.4% [0.5%, 2.4%] for natural, 2.2% [0.6%, 3.8%] for CVD, and 2.3% [−0.1%, 4.8%] for respiratory mortality per 10,166pt cm^{-3} increases in total PNC; and with Stölzel et al. (2007) in Erfurt (Germany) with increases in total mortality of 2.9% [0.3%, 5.5%] and in cardio-respiratory mortality of 3.1% [0.3%, 6.0%] per 9,748 for pt cm^{-3} increases. Although not comparable due to different methodologies (*meta*-analysis vs. time-series), Lanzinger et al. (2016) reported similar estimates for respiratory mortality (9.9% [−6.3%, 28.8%] per 2,750pt cm^{-3} increases in total PNC) in a study carried out in five central European cities. On the other hand, the estimates presented by Stafoggia et al. (2017) from a random-effects meta-analysis including eight European cities were much smaller than the estimates from the present study: they reported an increase in natural mortality of 0.35% [−0.05%, 0.75%] per 10,000pt cm^{-3} increases in total PNC.

As far as we are aware, no previous publication attempted to evaluate the effect on mortality from specific sources of UFP. However, some studies evaluated the associations with mortality of specific ranges of UFP. Both Braniš et al. (2010) and Halonen et al (2009) evaluated the associations between different size ranges representing the nucleation, Aitken and accumulation modes (ranges for Braniš et al. 2010: 15–49 nm, 49–205 nm, and 205–487 nm, respectively; ranges for Halonen et al. 2009: 10–30 nm, 30–100 nm, and 100–290 nm, respectively) and mortality and hospital admissions. They did not find associations

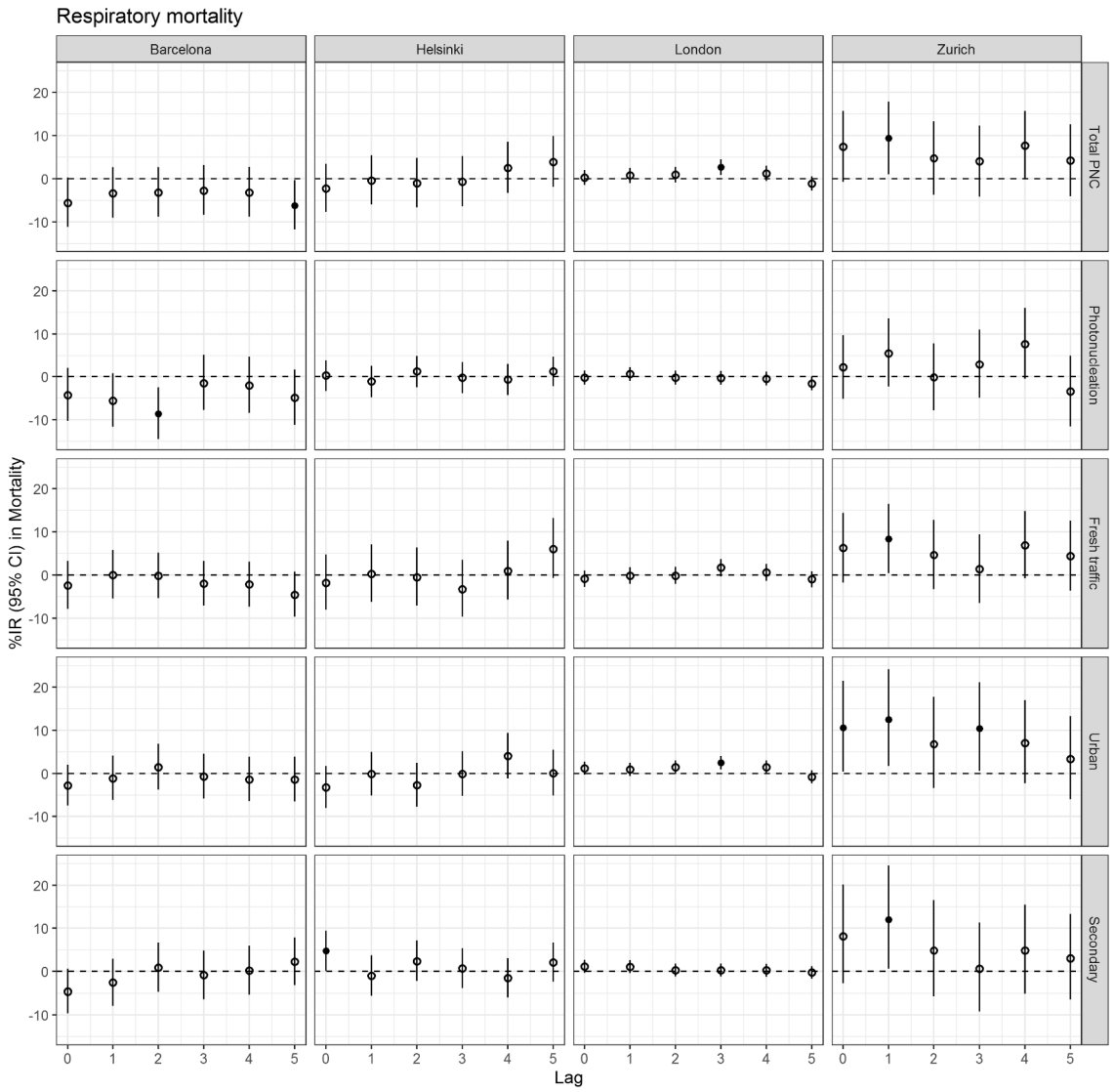

Fig. 3. Associations between respiratory mortality and total particle number concentrations (PNC) and the source contribution to ultrafine particles (photonucleation, fresh traffic, urban and secondary) from single lag models: percent increases of mortality (circles) and 95% confidence intervals (bars) per IQR increase at different lags.

between any of the size modes and mortality, but they found associations for respiratory admissions for the Aitken (20–100 nm, only Braniš et al. 2010) and accumulation modes (100–1000 nm). The short-lived atmospheric particles (i.e. nucleation particles) are likely less representative of exposure than the larger ones on moving away from the monitoring station because they show much higher spatial and temporal variability.

With the exception of Barcelona, the same pattern of associations for total PNC seemed to be followed by the fresh traffic source, for which we generally found the same associations and lags as for PNC. The fresh traffic source accounts, on average, for over 45% of the total PNC in all the cities and, thus, is one of the major sources of PNC in terms of number concentration. The fresh traffic source comprises traffic-emitted particles with the smallest particle size, and the fact that this source is showing many of the significant positive associations would be in accordance with the hypothesis of adverse health effects being enhanced with decreasing particle size (Meng et al., 2013). Also, the fresh traffic sourc has a major hydrocarbon component. Associations with the urban source can also be attributed to traffic emissions as, although it comprises a mix of other type of emissions such as biomass burning, aged traffic emissions are the main contributor to this source (Rivas et al., 2020).

In Barcelona, particles from photonucleation are very important in terms of source contribution to total PNC, especially during the warmer months (Brines et al., 2014; Pey et al., 2009; Reche et al., 2011; Rivas et al., 2020). An interesting result is the reduced risk of respiratory mortality in Barcelona (lag 2, −8.6% [−14.5%, −2.4%]) and CVD mortality in Helsinki (lag 1, −1.48 [−2.75, −0.21]) associated with photonucleation particles which may be attributed to the clean atmospheres (thus, low UFP from traffic emissions) needed for the photonucleation processes to take place (Brines et al., 2015; Spracklen et al., 2006). Another characteristic of the particles in the nucleation mode (<30 nm) is their short atmospheric lifetime, as these particles tend to quickly aggregate to form larger particles. Halonen et al. (2009) found that particles in the Aitken and Accumulation mode (>30 nm) were more consistently associated with hospital admissions and mortality than particles in the nucleation mode. The short atmospheric residence time of nucleation particles may complicate the exposure assessment and limit the capacity of the photonucleation particles to adversely affect the health of the population (Halonen et al., 2009). Moreover, the smallest particles measured at the monitoring station may not be representative of the exposure in the whole study area due to their

spatial variability.

The secondary source was also associated with an increased risk of natural and respiratory mortality in Helsinki (lag 5) and respiratory mortality in Zurich (lag 1 and 2). This source is comprised of particles in the accumulation mode which have longer residence times in the atmosphere and results in a longer period for exposure to these particles (Pellerin et al., 2017; Seinfeld and Pandis, 2006). The composition of these particles may vary considerably between cities, but they are often mainly comprised of ammonium-sulphate and ammonium-nitrate particles and condensable organic compounds (Rivas et al., 2020 and the references therein). Among the major components of the secondary organic aerosols (SOA) are the oxidised organic substances that have been reported to show high toxicity levels, particularly if they were generated from traffic/anthropogenic sources (as we would expect in these urban settings; Saffari et al., 2015; Tuet et al., 2017). We did not find an association with a biogenic source of SOA (related to emissions from vegetation; Rivas et al., 2020) that was only identified in Helsinki (Table S7). This would be in accordance with the higher toxicity being attributed to SOA with an anthropogenic origin.

In London, except for respiratory mortality, all the associations found were in the opposite direction to that expected. London is the largest city (in both area and population) and, therefore, where the highest exposure misclassification would be expected due to the high spatial variability of UFP (much larger than for fine particulate matter (PM; Lianou et al., 2007)). Previous studies reported that the temporal variation of 24-h average concentrations for PNC, but not the absolute concentrations, was well represented across the urban area by a central site (Puustinen et al., 2007). However, a different study showed correlations ranging from 0.18 to 0.45 between the 24-h average from a central site and outdoor and indoor concentrations in homes (Hoek et al., 2008). This exposure misclassification may affect all cities in this study, but due to its higher area, London may be the most affected (may show the highest spatial–temporal interaction). Another important characteristic of London data is the larger lower size cut of PNC (17 nm) which means that the smallest particles are not measured.

This study presents major strengths such as the comparison between cities with different characteristics and varied levels of UFP and related sources. The long time series available are also a major strength that provides the study with the appropriate statistical power.

Yet, this study presents the common limitations of epidemiological time-series studies. We estimated associations for multiple sources and lag times with three different mortality outcomes, therefore, some significant associations may have occurred purely by chance. Additionally, although we had long time series for ultrafine particles for most of the cities compared with other studies, missing data results in less statistical power and makes the interpretation more difficult. Another limitation is the difficulty of controlling for confounding of NO_2 and O_3 in the models because these pollutants were used in the source apportionment modelling. However, the adjusted models for total PNC seem to indicate that the patterns of association may remain stable. Moreover, as previously discussed for London, our exposure data was based on a single monitoring station, which may lead to exposure misclassification for a pollutant with as strong spatial heterogeneity such as UFP, especially for the smallest particles (e.g. photonucleation and fresh traffic sources). However, a previous study in Augsburg reported high temporal correlations of PNC across the city despite the high spatial variability, concluding that using data from a single station might be a proper approach in time-series epidemiologic analysis (Cyrys et al., 2008). A good correlation ($r = 0.74$) was also found between simultaneous PNC measurements in an urban background and a traffic site in Rome (Marconi et al., 2007). Even so, future research should benefit from the use of data obtained from several monitoring stations spread out over the area of study. Unfortunately, these data are not readily available for UFP and, therefore, our results bring the best information available on the associations between different sources of ultrafine particles and daily deaths from natural, cardiovascular, and respiratory causes.

5. Conclusion

In summary, we found inconsistent results across cities, sources and lags for associations with natural, cardiovascular, and respiratory mortality. The photonucleation source, which is usually observed under clean atmospheres, was associated with a reduced risk of mortality. Further research is needed to disentangle the inconsistencies of the effects of UFP on mortality and other health outcomes by overcoming the challenges related to this pollutant (e.g. spatial heterogeneity, physical dynamics).

CRediT authorship contribution statement

Ioar Rivas: Conceptualization, Methodology, Software, Formal analysis, Writing - original draft, Funding acquisition. **Laia Vicens:** Methodology, Software, Writing - review & editing. **Xavier Basagaña:** Methodology, Supervision, Writing - review & editing. **Aurelio Tobías:** Methodology, Writing - review & editing. **Klea Katsouyanni:** Conceptualization, Methodology, Supervision. **Heather Walton:** Methodology, Writing - review & editing. **Christoph Hüglin:** Resources, Writing - review & editing. **Andrés Alastuey:** Conceptualization, Resources, Writing - review & editing. **Markku Kulmala:** Conceptualization, Resources. **Roy M. Harrison:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Juha Pekkanen:** Writing - review & editing. **Xavier Querol:** Conceptualization, Methodology, Supervision, Resources, Writing - review & editing. **Jordi Sunyer:** Conceptualization, Methodology, Supervision, Writing - review & editing. **Frank J. Kelly:** Conceptualization, Supervision, Funding acquisition.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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This work was produced using statistical data from ONS. The use of the ONS statistical data in this work does not imply the endorsement of the ONS in relation to the interpretation or analysis of the statistical data. This work uses research datasets which may not exactly reproduce National Statistics aggregates.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2021.106662.

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